Treatment Failure in Tuberculosis Patient: The Role of Smoking Habit

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Abstract

Indonesia faces high burden of Tuberculosis (TB) each year. At the same time, smoking is considered to be common, especially in men. A number of TB patients, who receive standard regimen of TB therapy, would not easily give up on smoking, despite extensive advices from healthcare providers. This report aims to show evidence whether cigarette smoking increases the rate of treatment failure of standard anti-TB regiment in patients with pulmonary TB. Systematic search was done in two databases: Medline® and Scopus. Cohort studies were selected as appropriate study design to answer a prognosis question. Two cohort studies are found to be relevant with this report. Treatment failures upon standard regimen of TB therapy are 6.9% and 1.7% in both studies. Smoking habit has been demonstrated to increase the likelihood of treatment failure with OR 2.37 (95% CI: 1.24 – 4.54) and 7.489 (95% CI: 0.93 – 60.30). In conclusion, treatment failure in standard TB therapy is small. Smoking habit increases the treatment failure of standard anti-TB regiment in patients with pulmonary TB.

Keywords: *smoking, tuberculosis, treatment failure*

Peran Kebiasaan Merokok dalam Kegagalan Pengobatan Tuberkulosis

Abstrak

Setiap tahun Indonesia menghadapi beban tinggi tuberkulosis (TB) paru. Pada saat yang sama merokok dianggap sebagai kebiasaan umum, terutama pada populasi laki-laki dewasa. Penderita TB yang merokok cenderung tidak menghentikan kebiasaan buruknya walaupun sudah mendapat edukasi dari petugas kesehatan. Laporan kasus berbasis bukti ini bertujuan untuk menyajikan bukti bahwa merokok meningkatan kegagalan pengobatan TB pada penderita dalam regimen standar anti-TB. Pencarian sistematis dilakukan melalui database elektronik Medline® dan Scopus. Penelitian kohort dipilih sebagai jenis penelitian yang sesuai untuk menjawab pertanyaan prognosis pada studi ini. Terpilih dua penelitian berbasis kohort yang ditelaah dalam laporan ini. Dalam penelitian tersebut tingkat kegagalan pengobatan TB dengan regimen standar adalah 6,9% dan 1,7%. Kebiasaan merokok meningkatkan kegagalan pengobatan TB dengan OR 2,37 (95% CI: 1,24 – 4,54) dan 7,48 (95% CI: 0,93 – 60,3). Disimpulkan proporsi kegagalan pada terapi standar anti-TB tidak besar. Kebiasaan merokok meningkatan tingkat kegagalan pengobatan pada penderita TB.

Kata kunci: *merokok, tuberkulosis, gagal pengobatan*

Introduction

Tuberculosis (TB) remains a major leading cause of death in Indonesia, accounting of almost a tenth of all deaths.[1] Approximately 539.000 new cases of TB are accounted in yearly which make Indonesia ranks number five in the world.[2] This alarming number is coupled with the increasingly prevalent tobacco smoking in Indonesia.[3] In Indonesia, 65.9% of adult men smoke which contribute to total smokers of 34% of the population. Smoking is known to adversely affect clinical manifestations and disease progression of TB.[4] Another main concern is that smoking may be associated with poor adherence to TB treatment.

TB treatment failure subjects the patient for further time consuming and expensive treatment, with the concomitant risk for developing multi drugs-resistant TB (MDR-TB). TB management guideline used in Indonesia does not strongly emphasize on the importance of smoking cessation for TB patients.

The objective of this paper is to evaluate the effect of patients' smoking habit to TB treatment failure by means of appraising available medical evidences. The clinical question is "Does cigarette smoking increase the treatment failure of standard anti-TB regiment in patients with pulmonary tuberculosis (TB)?"

Clinical Case

An Indonesian 35 years old male came to Duren Sawit Primary Health Care Center (Puskesmas) with a chief complaint of chronic cough, accompanied with a slight reduction of body weight (from 55 kg to 53 kg in 1 month). History of night sweat and bloody cough was denied. The patient smokes two packs daily since he was 17 years old. His wife has been diagnosed with pulmonary tuberculosis (TB) one month prior. The patient's sputum examination revealed positive finding for acid fast bacilli. Consequently, standard anti-TB regimen therapy was immediately initiated. Despite the physician's advice to stop smoking, the patient continues to resume his deleterious habit.

Discussion

Two databases, Medline® and Scopus, were searched to identify studies evaluating the influence of cigarette smoking to TB treatment outcome. Eighty-three citations were identified from the searches, 72 from Medline® and 11 from Scopus. Two articles were finally included in this report based on the inclusion and exclusion criteria. Critical appraisal was performed utilizing the Oxford model of evidence based medicine.

Tachfouti et al,[5] performed a prospective cohort study to evaluate the impact of smoking on the failure rate of patients with TB. The trial was conducted in 15 TB control units (TCUs) in public primary and respiratory care centers in urban settings in Morocco. The diagnosis of TB was confirmed if the patients presented with symptoms of fever or cough and a sputum smear that showed acid-fast bacilli or a chest radiograph that showed changes compatible with a diagnosis of TB. A questionnaire was used to assess: (1) socio-demographic characteristics, (2) smoking status, and (3) alcohol consumption. All subjects in this study received combination anti-tuberculosis drug treatment and ancillary clinical care and follow-up for TB according to international guideline.[5] The study observed an overall proportion of treatment failure of 6.9%; it is significantly higher among smokers (9.1% vs. 4.5%; OR 2.37, 95% CI 1.24–4.54, p0<.01). There was no significant difference, however, between heavy and light smokers, or between non-smokers and passive smokers. After adjustment for socioeconomic variables (age and monthly income), clinical form of TB and alcohol consumption to exclude the possibility of confounding, smoking status remained significantly associated with treatment failure with aOR of 2.25 (95% CI 1.06-4.76; p<0.03).

Table 1. Assessment of Validity

Validity	Moroccan Tachoufti et al[6]	Malaysian Dujaili et al[7]
Was a defined, representative sample of patients assembled at a common (usually early) point in the course of their disease?	✓	✓
Was patient follow up sufficiently long and complete?	ü (30% loss to follow up)	✓
Were objective outcome criteria applied in a "blind" fashion?	×	Not mentioned
If subgroups with different prognoses are identified, was there adjustment for important prognostic factors?	✓	✓
Was there validation in independent group ("test-set") of patients?	✓	✓
Are the results of this prognosis study valid?	✓	✓

Tabel 2. Assessment of Importance

Importance	Proportion of Failure	Moroccan Dujaili et al[5]	Malaysian Dujaili et al[6]
How likely are the outcomes over time?	Overall failure	6.9%	1.7%
	In smoking	9.1%	2.9%
	In no smoking	4.5%	0.4%
	Risk difference (smoking – no smoking)	4.6%	2.5%
	crude OR	2.37	7.489
How precise are the estimate?	95% CI	(1.24 – 4.54)	(0.93 – 60.30)

Table 3. Assessment of Applicability

Applicability	Moroccan Dujaili et al[5]	Malaysian Dujaili et al[6]
Were the study patients similar to your own?	✓	✓
Will this evidence make a clinically important impact on your conclusions about what to offer or tell your patient?	✓	✓

Dujaili et al[6] performed a retrospective cohort study in Malaysia to determine the prevalence of smoking among TB patients in Penang and to compare the treatment outcomes between smoking and non-smoking TB patients. The subjects were grouped into either ever smokers (those who currently smoke cigarettes at the time of diagnosis of TB or who had previously quit smoking) or never smokers (those who never smoked or who have smoked less than 100 cigarettes during their lifetime). Unlike the trial in Morocco, the outcome measures evaluated in this study were: cured, treatment completion, treatment default, treatment failure and death. A TB patient is defined as cured if he/she is smear-negative at/or 1 month prior to the completion of treatment and on at least one previous occasion. In addition, a patient who has completed treatment but without proof of cure is considered as a case of treatment completion. A patient whose treatment was interrupted for 2 months or more is referred to as a case of treatment default, whereas death was defined as a patient who dies for any reason during the course of treatment. The patients' socio-demographic data, co-morbidities and clinical characteristics were collected by a retrospective review and assessment of the patients' medical records were carried out in order to evaluate treatment outcomes. In this study, ever-smoking TB patients were about seven times more likely to fail or default treatment (OR 7.489, 95% CI 0.93–60.30, p=0.039 and OR 7.176, 95% CI 2.76–18.62, p<0.001 respectively). They were also less likely to be cured from TB compared to never smokers (OR 0.342, 95% CI 0.21–0.49, p<0.001). After adjustment for the effects of confounders (age, sex, alcohol consumption, IVDU and history of chronic diseases including cyanotic heart disease, liver disease, chronic renal failure, malabsorption syndrome, cancer, steroids treatment and others), ever smokers were still significantly less likely to be cured (aOR 0.312, 95% CI 0.17–0.57, p<0.001) and more likely to default treatment (aOR 3.249, 95% CI 1.01–10.45, p<0.048). The risk of a smoker to die from TB or to fail treatment was statistically not significant (aOR 0.962, 95% CI 0.48-1.92, p=0.912 and aOR 13.593, 95% CI 0.59-308.69, p=0.101).

The evidence concerning the association of smoking status with undesirable TB treatment outcome (i.e. treatment failure) is consistent: Tachfouti et al[5] presented OR and aOR of 2.37 (95% CI 1.24–4.54, p<0.01) and 2.25 (95% CI 1.06-4.76; p<0.03), respectively; Dujaili et al[6] shown an OR of 7.489 (95% CI 0.93–60.3, p=0.039) and aOR of 13.593 (95% CI 0.59-308.69, p=0.101).

A number of important drawbacks are inherent in the critically appraised study. Tachfouti et al[5] encountered a high percentage of missing data, 19.2% drop out and 10.9% loss to follow-up (Table 2). This instance can distort the study results and subsequently its final conclusion. Dujaili et al[6] on the other hand, presented a very wide CI for the univariate assessment and multivariate binary logistic regression analysis of the association of tobacco smoking to treatment failure in TB patients.

A wide 95% CI indicates poor precision of the OR. It is also important to note that the 95% CI overlapped the null value both in univariate and multivariate analyses, thus they failed to reach statistical significance. Still, it does not prove absence of association between smoking status and rate of treatment failure.

Our patient is a smoker diagnosed with TB, now receiving anti-TB drug category I and refused to quit smoking. Based on two studies found, he will have poorer prognosis compared to non-smokers and more likely to fail or default treatment and less likely to be cured. Whether the likelihood of future outcomes will be altered if he quit smoking now is still a question. Nevertheless, smoking cessation have been proved to lower risk of cardiovascular, cerebrovascular, chronic obstructive pulmonary disease, and other pulmonary infections than TB.[8]

Conclusion

Smoking is associated with undesirable TB treatment outcome; treatment failure. Results from discussed trials suggested that smoking cessation may be beneficial to improve the success rate of TB treatment regiment and improve the patients' overall health.

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